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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/403,690	01/26/00	PFEFFER	K 20239-706

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EXAMINER	
EINSMANN,J	
ART UNIT	**PAPER NUMBER**
1655	13

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/403,690	PFEFFER, KLAUS	
	Examiner	Art Unit	
	Juliet C. Einsmann	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 September 2000* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

15)☒ Notice of References Cited (PTO-892)
16)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18)☐ Interview Summary (PTO-413) Paper No(s). _____ .
19)☐ Notice of Informal Patent Application (PTO-152)
20)☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of group A in Paper No. 12 is acknowledged. The traversal is on the ground(s) that the search and examination of all of the claims would not be a serious burden on the examiner. Applicant relies on the MPEP to support the assertion that the search and examination of up to ten oligonucleotide sequences is considered a reasonable number under MPEP 803.04. This is not found persuasive for the reasons that follow.

2. It is first to be noted that the instant restriction is between ten methods which are considered to be independent and distinct, not between only nucleotide sequences. The instant restriction is not based solely on the number of nucleotide sequences present in the claims. Searching of the instant claims involves more than just a search of a sequence but also a search of the prior art for the teaching concerning the use of the appropriate genes in the instant methods. The use of different genes in the methods in and of itself provides a sufficient burden for the separation of these inventions from one another. Furthermore, the discussion in MPEP section 803.04 is directed to a specific type of nucleic acid claim, and EST claim, where the claims are simply drawn to oligonucleotide sequences (see the examples in this section). The instant claims do not represent this type of sequence disclosure. However, assuming that they did meet that criteria, the directions set forth in the MPEP further states that "In some exceptional cases, the complex nature of the claimed material...may necessitate that the reasonable number of sequences to be selected be less than ten." In the instant case the fact that these sequences are from different genes and used in methods which include a broader search

than a simple sequence search this restriction is indeed considered to be appropriate. The requirement is still deemed proper and is therefore made FINAL.

Sequence Rules

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the following reason(s): The sequences are not properly identified with sequence identifiers in the claims. In order to comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825), Applicant must submit an amendment directing the insertion of the SEQ ID NOs into the appropriate pages of the specification.

Specification

3. The use of the trademark TaqMan™ has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

International Search Report

4. The references cited on the international search report and submitted with the pending application have been considered.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

> pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claim 16 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. MPEP 2163.06 notes "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. In re Rasmussen , 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)."

In the instantly rejected claims, the claiming of a kit appears to represent new matter. This application is a 371 of international application PCT/EP98/02341, which was published as WO98/48046, and it is this original specification which must provide basis for any amendments filed after the original filing date of 4/21/98. No specific basis for this limitation was identified in the applicant's response, nor did a review of the specification by the examiner find any basis for the limitation. Since no basis has been identified, the claims are rejected as incorporating new matter.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 2-9 13, 14, and 15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 2 and 3 are indefinite because it is not clear if the claim requires that the two primer pairs be selected from the "larger groups" listed or if the two primer pairs may be selected from any of those described, wherein the "larger groups" are the ones designated by a dash at the

beginning of the line. For example, it is not clear if the claim encompasses a method wherein, if the set contains only two primer pairs the two primer pairs could be one from heat labile toxin for enterotoxigenic E. coli and one from heat stabile toxin for enterotoxigenic E. coli, since these are in fact two different sets of primer pairs which would differentiate bacteria producing heat labile toxin versus heat stable toxin.

Claims 4-9 are indefinite over the recitation of "a fluorescent quencher dye which hybridises within the target DNA" because it is not clear if the quencher dye is intended to hybridize or if the previously mentioned oligonucleotide probe is intended to hybridize with the target DNA.

Claims 13, 14, 15, and 16 contain the trademark/trade name TaqMan™-PCR. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe a methodology using the PCR and a labeled probe and, accordingly, the identification/description is indefinite.

Claim Rejections - 35 USC § 102

9. NOTE: Claims 1, 4-5, 8-10, 13, and 16-20 were generic to all of the groups and are examined herein in as much as they correspond to the elected invention.

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 1, 2, 10, 11, 13, and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Lang *et al.* (Applied and Environmental Microbiology, Sept. 1994, p. 3145-3149).

Lang *et al.* teach a method for detection of pathogenic enterobacteria in a sample comprising PCR amplification of DNA isolated from said sample using a set of oligonucleotide primer pairs that allow the differentiation of enterotoxigenic and enterohemorrhagic E. coli strains by amplification of a toxin gene characteristic for the respective group of the pathogenic E. coli strains (p. 3146-3147). The LT (heat-labile) gene was used to detect enterotoxigenic E. coli, and the SLT I and SLT II genes were used to detect enterohemorrhagic E. coli. For use in their methods, Lang *et al.* a set of primers appropriate for their amplification method and a set of labeled probes useful to detect the amplified products (p. 3146).

Claim Rejections - 35 USC § 103

12. NOTE: Claims 1, 4-5, 8-10, 13, and 16-20 were generic to all of the groups and are examined herein in as much as they correspond to the elected invention.

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. Claims 3, 12, and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lang *et al.* in view of Yamamoto *et al.* (Journal of Bacteriology, Aug. 1983, Vol. 155, No. 2, p. 728-733) and further in view of Hogan *et al.* (US 5595874).

Lang *et al.* teach a method for detection of pathogenic enterobacteria in a sample comprising PCR amplification of DNA isolated from said sample using a set of oligonucleotide primer pairs that allow the differentiation of enterotoxigenic and enterohemorrhagic E. coli strains by amplification of a toxin gene characteristic for the respective group of the pathogenic E. coli strains (p. 3146-3147). The LT (heat-labile) gene was used to detect enterotoxigenic E. coli, and the SLT I and SLT II genes were used to detect enterohemorrhagic E. coli. Lang *et al.* further teach the primer sets necessary for this amplification and a set of probes useful to detect the amplified products.

Lang *et al.* do not teach methods or sets of primers and probes which include instant SEQ ID NO: 1, 2, or 19.

Yamamoto *et al.* teach the nucleotide sequence of heat labile toxin of E. coli pathogenic for humans (Figure 2). Instant SEQ ID NO: 1 consists of nucleotides 49-70 of this sequence, instant SEQ ID NO: 2 consists of the reverse complement of nucleotides 367-388 of this sequence, and instant SEQ ID NO: 78-104 of the sequence taught by Yamamoto *et al.* on pate 730.

Hogan et al. (US 5595874) teach the use of specific primers and furthermore provides specific guidance for the selection of primers,

> "At this point, the sequences are examined to identify potential probe regions. Two important objectives in designing a probe are to maximize homology to the target sequence(s) (greater than 90% homology is recommended) and to minimize homology to non-target sequence(s) (less than 90% homology to non-targets is recommended). We

> have identified the following useful guidelines for designing probes with the desired characteristics.
>
> First, probes should be positioned so as to minimize the stability of the probe:nontarget nucleic acid hybrid. This may be accomplished by minimizing the length of perfect complementarity to non-target organisms, avoiding G and C rich regions of homology to non-target sequences, and by positioning the probe to span as many destabilizing mismatches as possible (for example, dG:rU base pairs are less destabilizing than some others). Second, the stability of the probe:target nucleic acid hybrid should be maximized. This may be accomplished by avoiding long A and T rich sequences, by terminating the hybrids with G:C base pairs and by designing the probe with an appropriate Tm. The beginning and end points of the probe should be chosen so that the length and %G and %C result in a Tm about 2-10°C higher than the temperature at which the final assay will be performed. The importance and effect of various assay conditions will be explained further herein. Third, regions of the rRNA which are known to form strong structures inhibitory to hybridization are less preferred. Finally, probes with extensive self complementarity should be avoided (Col. 6, line 50-Col. 7, line 13)."

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have substituted primers and probes taken from the sequence taught by Yamamoto *et al.* in the methods taught by Lang *et al.* The ordinary practitioner would have been motivated to make such a substitution in order to have provided a method that is a functional equivalent of the method taught by Lang *et al.* in that both methods would be useful for the detection of enterotoxigenic E. coli. The teachings of Hogan *et al.* would have provided adequate direction to the ordinary practitioner in the selection of the probes and primers from the sequence taught by Yamamoto *et al.* In the absence of secondary considerations, such as unexpected results, the substitution of probes and primers selected using the guidance provided by Hogan *et al.* and the sequence provided by Yamamoto *et al.* into the methods taught by Lang *et al.* are obvious in view of the prior art.

15. Claims 4-6, 8 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lang *et al.* in view of Livak *et al.* (PCR Methods and Applications (1995) 4:357-362).

Lang *et al.* teach a method for detection of pathogenic enterobacteria in a sample comprising PCR amplification of DNA isolated from said sample using a set of oligonucleotide primer pairs that allow the differentiation of enterotoxigenic and enterohemorrhagic E. coli strains by amplification of a toxin gene characteristic for the respective group of the pathogenic E. coli strains (p. 3146-3147). The LT (heat-labile) gene was used to detect enterotoxigenic E. coli, and the SLT I and SLT II genes were used to detect enterohemorrhagic E. coli. For use in their methods, Lang *et al.* a set of primers appropriate for their amplification method and a set of labeled probes useful to detect the amplified products (p. 3146).

Lang *et al.* do not teach methods wherein a polymerase having 5'-3' exonuclease activity is used for the amplification of DNA and a probe labeled at both ends is used to detect amplified samples.

Livak *et al.* teach a PCR-based assay that uses the hydrolysis of an internal fluorogenic probe to monitor the amplification of the target (ABSTRACT). The method taught by Livak *et al.* utilizes a polymerase having 5'-3; exonuclease activity and a probe labeled at the 5' end with the fluorescent dye 6-carboxyfluorescein (6-FAM) and also labeled at the 3' end with the fluorescent quencher dye 6-carboxytetramethyl-rhodamine(TAMARA) (Fig. 2). The labeled probe hybridizes with the target DNA and is included in the amplification process.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have combined the methods taught by Lang *et al.* with those taught by Livak *et al.* The ordinary practitioner would have been motivated to use an assay such as the one taught by Livak *et al.* for the detection of E. coli since Livak *et al.* teach that such a method is a homogenous assay for detecting the accumulation of specific PCR products and probes with a

label attached to the 5' end and a quencher at the 3' end exhibit a large er signal in the 5' nuclease PCR assay than internally labeled probes (Abstract).

With regard to the specific PCR parameters discussed in claim 9, these are considered to be parameters obtained by routine optimization of an assay. As noted in *In re Aller*, 105 USPQ 233 at 235, "More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." Routine optimization is not considered inventive and no evidence has been presented that the PCR parameters claimed performed are other than routine, that the methods resulting from the optimization have any unexpected properties, or that the results should be considered unexpected in any way as compared to the closest prior art. As such, in the absence of a secondary consideration, such as unexpected results, these are considered obvious over the art of record.

16. Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lang *et al.* in view of Livak *et al.* as applied to claims 4-6, 8 and 9 above, and further in view of bothYamamoto *et al.* and Hogan *et al.*

The teachings of Lang *et al.* in view of Livak *et al.* are applied to claim 7 as they are applied to claims 4-6 above. Lang *et al.* in view of Livak *et al.* do not teach methods in which the probe used to detect the LT gene is SEQ ID NO: 19.

Yamamoto *et al.* teach the nucleotide sequence of heat labile toxin of E. coli pathogenic for humans (Figure 2). Instant SEQ ID NO: 78-104 of the sequence taught by Yamamoto *et al.* on pate 730.

Hogan et al. (US 5595874) teach the use of specific primers and furthermore provides specific guidance for the selection of primers,

> "At this point, the sequences are examined to identify potential probe regions. Two important objectives in designing a probe are to maximize homology to the target sequence(s) (greater than 90% homology is recommended) and to minimize homology to non-target sequence(s) (less than 90% homology to non-targets is recommended). We have identified the following useful guidelines for designing probes with the desired characteristics.
>
> First, probes should be positioned so as to minimize the stability of the probe:nontarget nucleic acid hybrid. This may be accomplished by minimizing the length of perfect complementarity to non-target organisms, avoiding G and C rich regions of homology to non-target sequences, and by positioning the probe to span as many destabilizing mismatches as possible (for example, dG:rU base pairs are less destabilizing than some others). Second, the stability of the probe:target nucleic acid hybrid should be maximized. This may be accomplished by avoiding long A and T rich sequences, by terminating the hybrids with G:C base pairs and by designing the probe with an appropriate Tm. The beginning and end points of the probe should be chosen so that the length and %G and %C result in a Tm about 2-10°C higher than the temperature at which the final assay will be performed. The importance and effect of various assay conditions will be explained further herein. Third, regions of the rRNA which are known to form strong structures inhibitory to hybridization are less preferred. Finally, probes with extensive self complementarity should be avoided (Col. 6, line 50-Col. 7, line 13)."

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have substituted primers and probes taken from the sequence taught by Yamamoto *et al.* in the methods taught by Lang *et al.* in view of Livak *et al.* The ordinary practitioner would have been motivated to make such a substitution in order to have provided a method that is a functional equivalent of the method taught by Lang *et al.* in view of Livak *et al.* in that both methods would be useful for the detection of enterotoxigenic E. coli. The teachings of Hogan *et al.* would have provided adequate direction to the ordinary practitioner in the selection of the probes and primers from the sequence taught by Yamamoto *et al.* In the absence of secondary considerations, such as unexpected results, the substitution of probes and primers selected using the guidance provided by Hogan *et al.* and the sequence provided by Yamamoto *et*

al. into the methods taught by Lang *et al.* in view of Livak *et al.* are obvious in view of the prior art.

17. Claim 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lang *et al.* in view of Livak *et al.* (PCR Methods and Applications (1995) 4:357-362) and further in view of the Stratagene Catalog.

Lang *et al.* teach a method for detection of pathogenic enterobacteria in a sample comprising PCR amplification of DNA isolated from said sample using a set of oligonucleotide primer pairs that allow the differentiation of enterotoxigenic and enterohemorrhagic E. coli strains by amplification of a toxin gene characteristic for the respective group of the pathogenic E. coli strains (p. 3146-3147). The LT (heat-labile) gene was used to detect enterotoxigenic E. coli, and the SLT I and SLT II genes were used to detect enterohemorrhagic E. coli. For use in their methods, Lang *et al.* a set of primers appropriate for their amplification method and a set of labeled probes useful to detect the amplified products (p. 3146).

Lang *et al.* do not teach methods wherein a a probe labeled at both ends, nor do they teach kits.

Livak *et al.* teach a PCR-based assay that uses the hydrolysis of an internal fluorogenic probe to monitor the amplification of the target (ABSTRACT). The method taught by Livak *et al.* utilizes a polymerase having 5'-3; exonuclease activity and a probe labeled at the 5' end with the fluorescent dye 6-carboxyfluorescein (6-FAM) and also labeled at the 3' end with the fluorescent quencher dye 6-carboxytetramethyl-rhodamine(TAMARA) (Fig. 2). The labeled probe hybridizes with the target DNA and is included in the amplification process.

Stratagene teaches gene characterization kits. The ordinary practitioner would have been motivated to have produced such a kit because since the Stratagene catalog expressly teaches the benefits to the practitioner of kits:

> "Each kit provides two services: 1) a variety of different reagents have been assembled and pre-mixed specifically for a defined set of experiments. When one considers all of the unused chemicals that typically accumulate in weighing rooms, desiccators, and freezers, one quickly realizes that it is actually more expensive for a small number of users to prepare most buffer solutions from the basic reagents. Stratagene provides only the quantities you will actually need, pre-mixed and tested. In actuality, the kit format saves money and resources for everyone by dramatically reducing waste. 2) The other service provided in a kit is quality control."

Therefore, the kits of the instant claims are *prima facie* obvious over the disclosure of Lang *et al.* in view of the Stratagene catalog.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have combined the methods taught by Lang *et al.* with those taught by Livak *et al.* The ordinary practitioner would have been motivated to use an assay such as the one taught by Livak *et al.* for the detection of E. coli since Livak *et al.* teach that such a method is a homogenous assay for detectign the accumulation of specific PCR products and probes with a label attached to the 5' end and a quencher at the 3' end exhibit a larger signal in the 5' nuclease PCR assay than internally labeled probes (Abstract). Further, in view of the teachings of the Stratagene Catalog, the ordinary practitioner would have been motivated to provide the reagents necessary to complete this assay in a kit. Therefore, the kit of the instant claim is *prima facie* obvious over the disclosure of Lang *et al.* in view of Livak *et al.* and further in view of the Stratagene catalog.

18. Claims 17 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lang *et al.* in view of Ohashi *et al.* (EP 0566504 A2).

Lang *et al.* teach a method for detection of pathogenic enterobacteria in a sample comprising PCR amplification of DNA isolated from said sample using a set of oligonucleotide primer pairs that allow the differentiation of enterotoxigenic and enterohemorrhagic E. coli strains by amplification of a toxin gene characteristic for the respective group of the pathogenic E. coli strains (p. 3146-3147). The LT (heat-labile) gene was used to detect enterotoxigenic E. coli, and the SLT I and SLT II genes were used to detect enterohemorrhagic E. coli. For use in their methods, Lang *et al.* a set of primers appropriate for their amplification method and a set of labeled probes useful to detect the amplified products (p. 3146). Lang *et al.* further teach that both ETEC and EHEC have been associated with the ingestion of food and are both known to be pathogenic to humans, causing symptoms including diarrhea.

Lang *et al.* do not teach methods in which these pathogenic bacteria are detected in samples derived from a human.

However, methods for the detection of pathogenic bacteria in samples derived from humans, such as clinical isolates from patients with diarrhea were routine in the art at the time the invention was made. Such a method for the detection of the LT gene of E. coli is exmplified by Ohashi *et al.* in Example 4 (p. 11, lines 9-10).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have used a method such as the one taught by Lang *et al.* in order to detect the presence of know pathogenic organisms in human samples. The ordinary practitioner would have been motivated to create such a method in order to provide a method for the diagnosis of E. coli infection in human patients.

19. Claims 17, 19, and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lang *et al.* in view of Tsen *et al.* (Journal of Food Protection (1996) Vol. 59, No. 8, pp. 795-802, ~~ABSTRACT ONLY~~).

Lang *et al.* teach a method for detection of pathogenic enterobacteria in a sample comprising PCR amplification of DNA isolated from said sample using a set of oligonucleotide primer pairs that allow the differentiation of enterotoxigenic and enterohemorrhagic E. coli strains by amplification of a toxin gene characteristic for the respective group of the pathogenic E. coli strains (p. 3146-3147). The LT (heat-labile) gene was used to detect enterotoxigenic E. coli, and the SLT I and SLT II genes were used to detect enterohemorrhagic E. coli. For use in their methods, Lang *et al.* a set of primers appropriate for their amplification method and a set of labeled probes useful to detect the amplified products (p. 3146). Lang *et al.* further teach that both ETEC and EHEC have been associated with the ingestion of food and are both known to be pathogenic to humans, causing symptoms including diarrhea.

Lang *et al.* do not teach methods in which these pathogenic bacteria are detected in consumables.

However, methods for the detection of pathogenic bacteria in consumables such as milk were routine in the art at the time the invention was made. Such a method for the detection of the LT gene of E. coli in milk is exmplified by Tsen *et al.* (ABSTRACT).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have used a method such as the one taught by Lang *et al.* in order to detect the presence of know pathogenic organisms in milk. The ordinary practitioner would have

been motivated to create such a method in order to provide a method for the screening milk samples for possible E. coli infections.

Conclusion

20. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Juliet C. Einsmann whose telephone number is (703) 306-5824. The examiner can normally be reached on Monday through Thursday, 7:00 AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 and (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Juliet C. Einsmann
Examiner
Art Unit 1655

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600

12/4/00

December 4, 2000